whereas the two cytoplasmic domain constructs were produced using the upstream primers (5'_3'):

GCC GAA TTC AAT GTA CAA GAC AAT CAT CAG T (SEQ ID NO: 103).

The latter two constructs were cloned into pFLAG-CMV-1 using EcoRI and KnpI sites. All constructs were verified by DNA sequencing on both strands. All expression constructs were shown to yield products of anticipated size in COS cells, after Western blot detection with M2 monoclonal antibody (not shown).--

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REMARKS

A. The Specification has been Amended to Identify the Sequences in FIG. 7 and FIG. 14

The Communication dated April 23, 2001, states that Applicants' response to the Office Action dated August 1, 2000, failed to comply with the sequence rules in that the sequences in FIG. 7 and FIG. 14 are not identified by their corresponding SEQ ID NO:. The specification has been amended to recite the SEQ ID NOs: in FIG. 7 and FIG. 14. For the convenience of the Examiner, Appendix A is attached hereto containing a marked-up version of the amendments to the specification made herein.

B. A Substitute Sequence Listing is Being Submitted

Applicants stated, in their response filed February 7, 2001, to the Office Action dated August 1, 2000, that a substitute Sequence Listing containing the sequence for J-Toll 4 shown in FIGS. 7A-7B and the sequences provided in the description of FIG. 14 at page 18, lines 7, 9, 14 and 17, would be provided. A substitute Sequence Listing which includes these sequences is attached hereto as Appendix B. Also submitted herewith is a computer readable format thereof and a statement as required by 37 CFR § 1.825(a) and (b) and statement as required by 37 CFR §

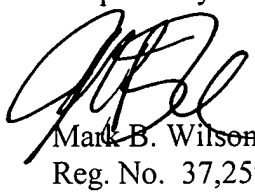
1.825(g), is submitted herewith. Applicants represent that no new matter is added by this submission.

C. Conclusion

Applicants believe this paper to be a full and complete response to the Communication dated April 23, 2001, and the Office Action dated August 1, 2000. Should the Examiner have any comments or questions with regard to any statements contained herein, the Examiner is respectfully requested to contact the Applicants' representative listed below.

Please date-stamp and return the enclosed postcard evidencing receipt of these materials.

Respectfully submitted,



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Date: May 23, 2001

APPENDIX A

Marked-Up Version of Amendments to Specification

FIG. 7A. Amino acid sequence of mouse mutant J-Toll-4 (SEQ ID NO: 104), mouse N-Toll-4 (SEQ ID NO: 99), rat TLR-4 (SEQ ID NO: 6) and human TLR-4 (SEQ ID NO: 2). The mutant mouse J-toll TLR-4 amino acid sequence contains a point mutation at residue 712 (proline to histidine), not found in the amino acid sequences of N-Toll-4, rat TLR-4 or human TLR-4. The numbering system in this figure does not take into account the spacing to maximize the sequence alignment.

FIG. 14. Schematic illustration of recombinant proteins expressed in RAW 264.7 cells. Constructs were made by PCR, using cDNA derived from C3H/HeJ and C3H/HcN mice. The primers (5'_3'):

ATC GAT ACC AGG AGG CTT GAA TCC C (SEQ ID NO: 100)

and

TAT CGA TAC CAG GAA GCT TGA ATC CC (SEQ ID NO: 101)

were used to generate the full-length amplified products, which were cloned into the vector pFLAG-CMV-1 (Sigma) using ClaI and KpnI sites. The native signal peptide was thus removed, and an alternative signal peptide, followed by the flag sequence, was provided by the vector. The ectodomain construct was produced using the downstream primer (5'_3'):

CAG GGT ACC TCA CAG GTG AAA ATA GAA GTG GTA T (SEQ ID NO: 102),

whereas the two cytoplasmic domain constructs were produced using the upstream primers (5'_3'):

GCC GAA TTC AAT GTA CAA GAC AAT CAT CAG T (SEQ ID NO: 103).

The latter two constructs were cloned into pFLAG-CMV-1 using EcoRI and KnpI sites. All constructs were verified by DNA sequencing on both strands. All expression constructs were shown to yield products of anticipated size in COS cells, after Western blot detection with M2 monoclonal antibody (not shown).